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A SELECTIVE CLEAVAGE OF AROMATIC BENZYL ETHERS LOCATED ORTHO TO A CARBONYL GROUP BY MAGNESIUM BROMIDE.

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Abstract. The selective debenzylation of various aromatic dibenzyloxy aldehydes by magnesium bromide in anhydrous ether-benzene solution by a gentle reflux for 36 hours is described. Only benzyloxy groups located ortho to the carbonyl group were cleaved cleanly and highly efficiently, leaving other benzyl ether groups unaffected. A six-membered chelation ring intermediate is proposed. The preparation of all relevant dibenzyloxy napthalene and benzene aldehyde precursors is described by benzylation of the corresponding diols and, usually, a subsequent Vilsmeier formylation.

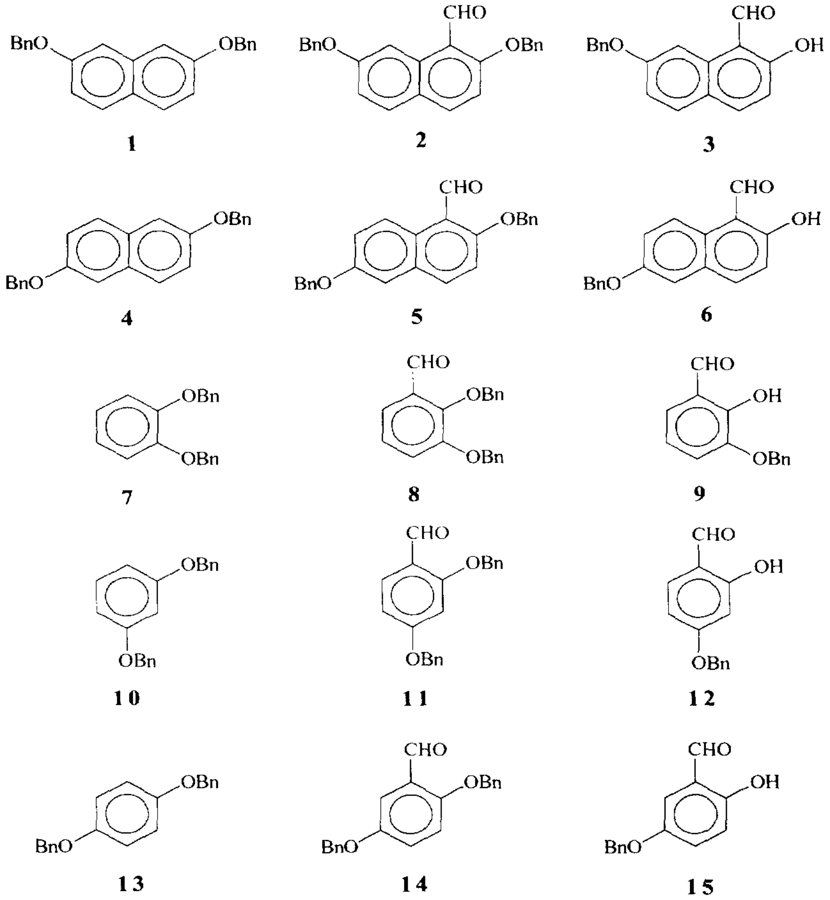
INTRODUCTION

Protective groups play a crucial role in modern multi-step synthetic organic chemistry[1-4]. There is no doubt that the immense achievements over the past decades in the highly selective construction of various polyfunctional molecules such as alkaloids, prostaglandins, nucleotides, oligosaccharides, macrolides and polyether antibiotics were not possible without the extensive use of protecting groups. This is particularly eminent in carbohydrate and nucleotide chemistry involving the selective protection and deprotection of a specific hydroxyl group in the presence of several others of very similar or comparable reactivity. Ethers have been widely used as stable protective groups for the hydroxyl group in organic synthesis[5]. In this relation benzyl ethers are among the most versatile owing to their ease of formation, inherent stability and variety of available deprotection methods, including Lewis acids, catalytic hydrogenolysis, dissolving metal reduction and oxidation[2].

This paper describes a highly selective cleavage of benzyl ethers located ortho to an aldehydic carbonyl group in various benzene and napthalene derivatives along with their preparation[6]. This was effected by magnesium bromide in an ethereal benzene solution and involves the formation of a six-membered chelation ring. The reactions proceeded highly efficiently, usually in good to excellent yields, and other benzyloxy groups present in the molecule were not affected. Such selectivity is a highly desirable feature of an ether cleavage agent and it is believed that it may offer various beneficial prospects to synthetic organic chemistry. More reactive Lewis acids such as aluminum and boron trichlorides were found to offer no selectivity and cleaved all benzyl ethers present. Magnesium bromide has previously been employed to selectively deprotect THP ethers of primary and secondary alcohols[7] and 1-ethoxyethyl ethers[8] as well as deprotecting acetal esters[9].

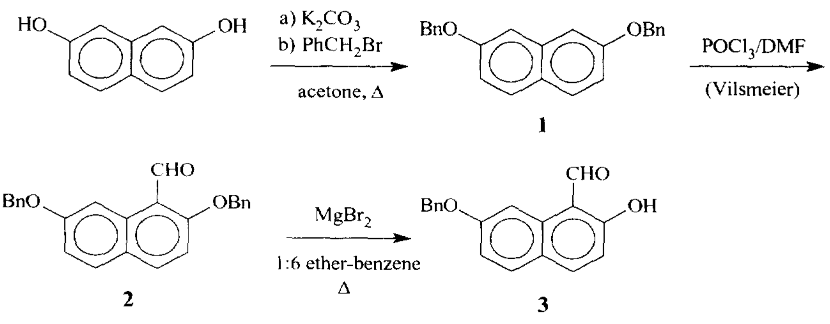
RESULTS AND DISCUSSION

Various aromatic naphtalene and benzene aldehyde derivatives possessing two benzyl groups, a neighbouring one located ortho to the carbonyl group, and a distant one with no such relationship, were prepared and investigated. Unless otherwise stated, they were prepared from dihydroxy precursors. All relevant napthalene and benzene intermediary derivatives and products **1** - **15**, are listed in Scheme 1.



Scheme 1

A typical overall process involving the selective deprotection is depicted in Scheme 2 for 2,7-dibenzyloxynapthalene, **1**, which was used as a demonstrative model system. It consists of benzylation of 2,7-dihydroxynapthalene, a subsequent Vilsmeier formylation and, finally, a selective debenzylation of the resulting 2,7-dibenzyloxy-1-napthaldehyde, **2**, by magnesium bromide[10] to afford **3**. Below, each reaction is described and some of their characteristic features discussed briefly.



Scheme 2

Benzylation

The dibenzyloxy derivatives **1**, **4**, **7**, **10** and **13** were generally obtained by treatment of the corresponding dihydroxy napthalene and benzene derivatives with benzyl chloride in boiling acetone in the presence of potassium carbonate as a base. The reactions were allowed to proceed for 36 hours and the products were usually obtained in good yields, apart from **4** which was obtained in only 39 % yield.

Vilsmeier Formylation

An attempted Vilsmeier formylation of **1** by a procedure reported by Hoó and Lavit[11] for 2,7-dimethoxynapthalene resulted in a very dark solution from which no product could be isolated. Their procedure involved simply mixing the reagents together simultaneously. A modified procedure involving a separate preparation of the Vilsmeier reagent, to which **1** was added, resulted in a clean, high-yielding reaction. That modified procedure was then used to convert compounds **4** and **10** into the corresponding aldehydes, **5** and **11**, in fair and excellent yields, respectively.

The corresponding formylation of **7** and **13** to form **8** and **14**, respectively, failed, presumably as a result of mismatching directing effects of the ortho and para interrelated benzyloxy groups. For compound **10** this was not a problem, since the directing effects of the meta interrelated benzyloxy groups reinforced each other. In compounds **1** and **4** the formylation took readily place into the more activated α-positions of the napthalene periphery.

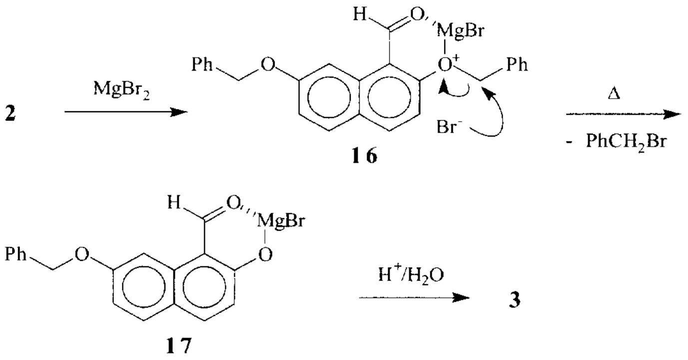
Alternatively, derivatives **8** and **14** were readily obtained from the commercially available 2,3- and 2,5-dihydroxybenzaldehyde adducts by benzylation with benzyl chloride in dry DMSO using sodium hydride as a base. The reactions proceeded in very high yields, but the previously described benzylation procedure in acetone with potassium carbonate had failed and aldol condensation products were obtained.

The proton NMR spectra of the napthaldehyde compounds **2** and **5** warrant a special comment. Their H_8 protons were substantially deshielded as compared to the corresponding protons in their precursors due to a *peri* interaction[12] with the 1-formyl group. After a successful deprotection the formyl group underwent a strong hydrogen bonding over a six-membered ring. Since the carbonyl group is now fixed into a position where its deshielding zone influences the chemical shift of H_8 to a far less extent, the consequence was a considerable up-field shift in protons H_8 in the products.

Debenzylation with Magnesium Bromide

The selective debenzylation reaction with magnesium bromide took place under a reflux in a 1:6 mixture of ether in benzene highly efficiently in good to excellent yields. Such selective deprotections are well established for other Lewis acids. Boron trichloride, for instance, is known to selectively deprotect the more stable aromatic methoxy groups adjacent to a carbonyl function in a manner analogous to the one described in the present work[13], whereas the more reactive boron tribromide or magnesium iodide do not normally show such selectivity[3].

The reaction is believed to take place by the mechanism shown in Scheme 3 for compounds **2** and **3**. The metal halide initially coordinates with the oxygen atoms of the carbonyl group and the benzyl ether ortho to the carbonyl group forming the six-membered chelation ring intermediate **16**. This is followed by a nucleophilic attack of the benzylic carbon by bromide in forming complex **17**, which, although isolable as a yellow moisture-sensitive solid, was not characterized. Hydrolysis of **17** led to the product **3**. That an intermediate of the type **16** was indeed involved is supported by the fact that immediately after the addition of magnesium bromide to solution of **2** a green-yellow complex was formed. When that complex was stirred overnight at room temperature no change in colour occurred and hydrolysis at this stage led to a quantitative recovery of starting material. On the other hand, when **16** was very gently refluxed a change in colour occurred, presumably as a result of formation of **17**. Hydrolysis then gave the desired product.



Scheme 3

CONCLUSION

Various benzene and naphthalene dibenzyloxy aldehyde derivatives were prepared in an efficient manner and usually in good yields. Their magnesium bromide mediated debenzylation reactions took place very efficiently and highly selectively in good to excellent yields by a gentle reflux under anhydrous conditions in an ethereal benzene mixture. It is believed that the presence of a coordinating cosolvent such as ether in the reaction medium may play a crucial role in mediating the selectivity of magnesium bromide as an ether cleaving agent. This is currently under investigation in relation to various Lewis acid sensitive hydroxyl protection groups and it is anticipated that magnesium bromide may further contribute to the chemistry of protective groups and thus synthetic organic chemistry.

EXPERIMENTAL

Melting points were determined on a Büchi 520 melting point apparatus and are uncorrected. ^1H and ^{13}C nuclear magnetic resonance spectra were recorded at 300 and 75.4 MHz, respectively, on a Bruker WH300 instrument in deuterated chloroform using tetramethylsilane as an internal reference for the proton spectra. Infrared spectra were conducted on a Perkin-Elmer 283 Infrared Spectrophotometer. Microanalysis and mass spectrometric analysis were performed at the Dyson Perrins Laboratory, Oxford, U.K. All dihydroxynapthalene and benzene derivatives and the dihydroxybenzaldehyde derivatives were purchased from Aldrich Chemical Company in U.K. Benzyl chloride and sodium hydride as 80 % dispersion in mineral oil were also purchased from Aldrich Chemical Company. All other reagents and chemicals as well as all solvents used were supplied by Merck in Darmstadt. Diethyl ether, benzene, toluene, DMF and DMSO were dried and freshly distilled prior to use by standard methods[14]. Acetone, chloroform, dichloromethane and n-hexane were analytical reagent grade. Bromine was purified in accordance with standard methods by refluxing over potassium bromide, distillation, washing with concentrated sulfuric acid and redistillation[14]. Yields are in all cases based on isolated and purified crystalline material.

2,7-Dibenzyloxynaphtahlene, **1**.

To a mixture of dry acetone (1.0 l) and ground anhydrous potassium carbonate (300 g, 2.15 mol) was added 2,7-dihydroxynaphthalene (150 g, 0.938 mol). The mixture was stirred efficiently at reflux for 1 hour. Benzyl chloride (274 g, 250 ml, 2.15 mol) was added in one lot to the mixture which was then refluxed for 36 hours. The solution was allowed to cool down and filtered. The collected solid was washed with ethanol and then added to a 1 M aqueous NaOH solution (1.0 l), filtered, and washed several times with 1 M aqueous NaOH, then water and finally with ethanol. This gave, after drying, a white crystalline product (160 g). The acetone solvent was evaporated from the original filtrate and ethanol was added to the dark-green residue. The precipitate was collected by filtration and washed several times with ethanol followed by 1 M aqueous NaOH, water and finally ethanol. The off-white material was dried and combined with the first crop (240 g, 75 %). Recrystallization from chloroform (900 ml) after treatment with active carbon afforded large colourless crystals, m.p. 159.0 - 160.0 °C. Repeated recrystallization from chloroform afforded the analytical sample. Elemental analysis. Found: C, 84.45; H, 5.83. $C_{24}H_{20}O_2$ requires C, 84.68; H, 5.92 %. ν_{max} ($CHCl_3$) 3010 (m, C-H), 1630 (vs, ar), 1605 (s, ar), 1512 (vs, ar), 1450 (vs, ar), and 1253 (vs, C-O-C) cm^{-1}. δ ^1H ($CDCl_3$) 5.10 (s, 4H, 2x $-CH_2Ph$), 7.11 (dd, J = 2.3 and 8.8 Hz, 2H, H_3 and H_6), 7.15 (d, J = 2.3 Hz, 2H, H_1 and H_8), 7.36 - 7.52 (m, 10 H, 2x $-C_6H_5$), 7.69 (d, J = 8.8 Hz, 2H, H_4 and H_5) ppm. δ ^{13}C ($CDCl_3$) 70.0, 106.8, 116.5, 124.6, 127.5, 127.9, 128.5, 129.2, 135.8, 137.0, 157.4 ppm. m/e (EI) 340 (M^+, 15), 91 (100 %) amu.

2,7-Dibenzyloxy-1-naphthaldehyde, **2**.

To an ice-cooled flask containing dry, freshly distilled DMF (10 ml, about 4 equivalents) was added, with stirring, distilled $POCl_3$ (4.60 g, 2.80 ml, 0.030 mol) over a period of 30 minutes. A further volume of DMF (10 ml) was added together with toluene (10 ml). 2,7-Dibenzyloxynaphthalene, **1**, (10.0 g, 0.029 mol) was added as a solid and the solution allowed to warm up to room temperature and then stirred efficiently overnight. This resulted in a greenish-yellow nonhomogeneous solution. The reaction mixture was heated gradually up to 100 °C over 5 hours and kept at that temperature for a further hour. The homogeneous light-brown solution was poured into water (50 ml) saturated with sodium acetate trihydrate (35 g) and then boiled for 30 minutes. A brownish solid formed on cooling. The mixture was extracted with dichloromethane (2x 50 ml) and the combined aqueous extracts were evaporated *in vacuo*. The residue was crystallized from ethanol (50 ml) affording **2** as a yellowish crystalline material (9.60 g, 89 %). Subsequent recrystallization from ethanol gave very pale-yellow, glistening crystals, m.p. 110 - 115 °C. Elemental analysis. Found: C, 81.69; H, 5.48. $C_{25}H_{20}O_3$ requires C, 81.50; H, 5.47 %. ν_{max} ($CHCl_3$) 3010 (s, C-H), 1665 (vs, C=O), 1618 (vs, ar), 1595 (s, ar), 1510 (vs, ar) and 1450 (s, ar) cm^{-1}. δ ^1H ($CDCl_3$) 5.26 (s, 2H, $-CH_2Ph$), 5.32 (s, 2H, $-CH_2Ph$), 7.16 (dd, J = 2.4 and 8.9 Hz, 1H, H_6), 7.36 - 7.57 (m, 11H, 2x $-C_6H_5$ and H_3), 7.68 (d, J = 8.9 Hz, 1H, H_5), 7.95 (d, J = 9.0 Hz, 1H, H_4), 9.00 (d, J = 2.4 Hz, 1H, H_8) and 10.99 (s, 1H, -CHO) ppm. δ ^{13}C ($CDCl_3$) 69.9, 71.2, 104.7, 110.8, 117.7, 124.2, 127.3, 127.4, 127.8, 127.9, 128.2, 128.4, 128.6, 129.7, 133.3, 135.9, 136.6, 137.1, 160.5, 163.9 and 191.8 ppm. m/e (EI) 368 (M^+, 23), 369 (6), 340 (3), 277 (12) and 91 (100 %) amu.

7-Benzyloxy-2-hydroxy-1-naphthaldehyde, **3**.

To magnesium turnings (7.5 g, 0.308 mol, 2 equivalents) was added anhydrous ether (150 ml) and dry benzene (150 ml). The flask was cooled to 0 °C, and bromine (26.32 g, 8.51 ml, 0.165 mol) was then added carefully. When the reaction had started (effervescence after the addition of a few drops of bromine), stirring was commenced and the addition of bromine continued until complete. The ice-bath was removed and the solution was first refluxed gently for several minutes, until the solution was almost colourless, and then allowed to cool. The magnesium bromide solution was then slowly added to 2,7-dibenzyloxy-1-naphthaldehyde, **2**, (60.0 g, 0.163 mol) in dry benzene (750 ml) at room temperature. During the transfer the reaction mixture was stirred very efficiently. A green-yellow precipitate was formed instaneously and upon completion of addition the mixture was stirred at room temperature overnight. The reaction mixture was then gently refluxed on a steam-bath for 36 hours. By the end of that period the colour had turned to yellow. The mixture was allowed to cool, filtered and washed with benzene. The yellow magnesium complex was transfered to an aqueous 1 M HCl solution (1.0 l) and boiled for 30 minutes. A light-brown mass came out of solution when allowed to cool. The mixture was extracted with dichloromethane (2x 400 ml). The combined extracts were dried over Na_2SO_4 and concentrated to dryness. The crude product was recrystallized from ethanol (750 ml) after treatment with active carbon, affording a pale-yellow crystalline compound (21.72 g, 70 %). Recrystallization from ethanol afforded the analytical sample, m.p. 123.0 - 125.0 °C. Elemental analysis. Found: C, 77.57; H, 5.23. $C_{18}H_{14}O_3$ requires C, 77.68; H, 5.07 %. ν_{max} ($CHCl_3$) 3600 - 2400 (w, br, O-H), 3020 (m, C-H), 1625 (vs, C=O), 1590 (s, ar), 1512 (s, ar), 1450 (s, ar) and 1240 (s, C-O-C) cm^{-1}. δ ^1H ($CDCl_3$) 5.23 (s, 2H, $-CH_2Ph$), 6.97 (d, J = 8.9 Hz, 1H, H_3), 7.16 (dd, J = 2.2 and 8.9 Hz, 1H, H_6), 7.37 - 7.51 (m, 5H, $-C_6H_5$), 7.71 (d, J = 8.9 Hz, 1H, H_5), 7.73 (d, J = 2.2 Hz, 1H, H_8), 7.88 (d, J = 8.9 Hz, 1H, H_4), 10.67 (s, 1H, -CHO) and 13.17 (s, 1H, -OH) ppm. δ ^{13}C ($CDCl_3$) 70.1, 100.4, 110.7, 115.7, 116.3, 123.0, 127.3, 128.1, 128.6, 130.9, 134.6, 136.3, 138.7, 159.3, 165.4 and 192.5 ppm. m/e (EI) 278 (M^+, 13), 279 (2.5) and 91 (100 %) amu.

2,6-Dibenzyloxynaphthalene, **4**.

4 was afforded in only 39 % yield by a procedure identical to the one described for **1**. Recrystallization from chloroform afforded white crystals, m.p. 172.0 - 173.0 °C. Elemental analysis. Found: C, 84.57; H, 5.80. $C_{24}H_{20}O_2$ requires C, 84.68; H, 5.92 %. ν_{max} (KBr) 3060 - 3020 (m, C-H), 2930 - 2910 (m, C-H), 1600 (vs, ar), 1510 (s, ar), 1455 (vs, ar) and 1225 (vs, C-O-C) cm^{-1}. δ ^1H ($CDCl_3$) 5.17 (s, 4H, 2x $-CH_2Ph$), 7.21 - 7.52 (m, 14H, 2x $-C_6H_5$, H_3, H_4, H_7 and H_8), 7.66 (d, J = 8.7 Hz, 2H, H_4 and H_8) ppm. m/e (EI) 340 (M^+, 23), 341 (5), 91 (100 %) amu. Accurate mass. Found: 340.1463; $C_{24}H_{20}O_2$ requires 340.1463 amu.

2,6-Dibenzyloxy-1-naphthaldehyde, **5**.

5 was afforded in 52 % yield by a procedure identical to the one described for **2**. Recrystallization from ethanol afforded analytically pure material as bright green-yellow crystals, m.p. 94.0 - 95.0 °C. Elemental analysis. Found: C, 81.27; H, 5.33. $C_{25}H_{20}O_3$ requires C, 81.50; H, 5.47 %. ν_{max} ($CHCl_3$) 3100 - 3000 (m, C-H), 2920 (m, C-H), 1660 (vs, C=O), 1595 (vs, ar), 1510 (s, ar), 1450 (s, ar) and 1250 (vs, C-O-C) cm^{-1}. δ ^1H ($CDCl_3$) 5.18 (s, 2H, $-CH_2Ph$), 5.32 (s, 2H, $-CH_2Ph$), 7.18 (d, J = 2.7 Hz, 1H, H_5), 7.33 (d, J = 9.0 Hz, 1H, H_3), 7.37 - 7.48 (m, 11H, 2x $-C_6H_5$ and H_7), 7.93 (d, J = 9.0 Hz, 1H, H_4), 9.23 (d, J = 9.3 Hz, 1H, H_8) and 10.95 (s, 1H, -CHO) ppm. m/e (EI) 368 (M^+, 13), 369 (3.5), 340 (5) and 91 (100 %) amu. Accurate mass. Found: 368.1410; $C_{25}H_{20}O_3$ requires 368.1412 amu.

6-Benzyloxy-2-hydroxy-1-naphthaldehyde, **6**.

6 was afforded in 63 % yield by a procedure identical to the one described for **3**. Recrystallization from ethanol afforded a green yellowish crystalline material, m.p. 156 - 159 °C. Elemental analysis. Found: C, 77.49; H, 4.84. $C_{18}H_{14}O_3$ requires C, 77.68; H, 5.07 %. ν_{max} (KBr) 3600 - 2400 (w, br, O-H), 3020 (m, C-H), 2900 (m, C-H), 1625 (vs, C=O), 1595 (vs, ar), 1520 (s, ar) and 1455 (s, ar) cm^{-1}. δ ^1H ($CDCl_3$) 5.18 (s, 2H, $-CH_2Ph$), 7.14 (d, J = 9.1 Hz, 1H, H_3), 7.24 (d, J = 2.7 Hz, 1H, H_5), 7.40 (dd, J = 2.7 and 9.2 Hz, 1H, H_7), 7.36 - 7.48 (m, 5H, $-C_6H_5$), 7.89 (d, J = 9.1 Hz, 1H, H_4), 8.29 (d, J = 9.2 Hz, 1H, H_8), 10.79 (s, 1H, -CHO) and 12.92 (s, 1H, -OH) ppm. m/e (EI) 278 (M^+, 24), 279 (5.3) and 91 (100 %) amu. Accurate mass. Found: 278.0943; $C_{18}H_{14}O_3$ requires 278.0943 amu.

1,2-Dibenzyloxybenzene, **7**.

7 was afforded in 72 % yield by a procedure identical to the one described for **1**. Recrystallization from ethanol afforded white crystalline flakes, m.p. 57.5 - 58.0 °C. Elemental analysis. Found: C, 82.71; H, 6.35. $C_{20}H_{18}O_2$ requires C, 82.73; H, 6.25 %. ν_{max} ($CHCl_3$) 3060 - 3000 (m, C-H), 2920 (m, C-H), 1590 (s, ar), 1500 (vs, ar), 1450 (s, ar) and 1250 (vs, C-O-C) cm^{-1}. δ ^1H ($CDCl_3$) 5.18 (s, 4H, 2x $-CH_2Ph$), 6.88 - 6.98 (m, AA'BB', 4H, H_3, H_4, H_5, H_6), 7.31 - 7.48 (m, 10H, 2x $-C_6H_5$) ppm. m/e (EI) 290 (M^+, 31), 291 (7.9), 199 (9) and 91 (100 %) amu. Accurate mass.

Found: 290.1306; $C_{20}H_{18}O_2$ requires 290.1307 amu.

2,3-Dibenzyloxybenzaldehyde, **8**.

To a stirred solution of 2,3-dihydroxybenzaldehyde (2.50 g, 18.3 mmol) in DMSO (30.0 ml) at room temperature under nitrogen was added sodium hydride (80 % dispersion in mineral oil; 1.13 g, 37.5 mmol). The solution was stirred at r.t. for 15 minutes after which benzyl chloride (4.75 g, 4.33 ml, 37.5 mmol) was added. The mixture was then stirred for 15 hours. The DMSO solution was treated once with n-pentane (10 ml) in a separatory funnel. Then, water was added to the DMSO phase and extracted with dichloromethane (2x 100 ml). The combined organic phases were washed with water (3x 100 ml), 1.0 M NaOH (100 ml) and water (100 ml), dried over magnesium sulfate and the solvent removed *in vacuo* to afford **8** as an off-white crystalline material (4.70 g, 87 %). Recrystallization from ethanol afforded analytically pure material as white fine needles, m.p. 90.5 - 91.5 °C. Elemental analysis. Found: C, 79.36; H, 5.66. $C_{21}H_{18}O_3$ requires C, 79.22; H, 5.70 %. ν_{max} (KBr) 3030 (w, C-H), 1695 (vs, C=O), 1585 (s, ar), 1500 (s, ar), 1480 (s, ar), 1455 (s, ar) and 1250 (vs, C-O-C) cm^{-1}. δ ^1H ($CDCl_3$) 5.20 (s, 2H, -CH_2Ph), 5.21 (s, 2H, -CH_2Ph), 7.13 (t(dd), J = 8.0 Hz, 1H, H_5), 7.25 (dd, J = 1.6 and 8.0 Hz, 1H, H_4), 7.33 - 7.50 (m, 10H, 2x -C_6H_5), 7.42 (dd, J = 1.6 and 9.0 Hz, 1H, H_6) and 10.27 (s, 1H, -CHO) ppm. δ ^{13}C ($CDCl_3$) 71.4, 76.5, 119.7, 120.0, 124.2, 127.5, 128.3, 128.5, 128.5, 128.5, 128.7, 128.7, 130.6, 136.3, 151.6, 152.2 and 190.1 ppm. m/e (EI) 318 (M^+, 1.3), 227 (15) and 91 (100 %) amu. Accurate mass. Found: 318.1253; $C_{21}H_{18}O_3$ requires 318.1256 amu.

3-Benzyloxy-2-hydroxybenzaldehyde, **9**.

9 was afforded in 95 % yield by a procedure identical to the one described for **3**. Recrystallization from ethanol afforded yellowish needles, m.p. 88.0 - 88.5 °C. Elemental analysis. Found: C, 73.95; H, 5.18. $C_{14}H_{12}O_3$ requires C, 73.67; H, 5.30 %. ν_{max} (KBr) 3600 - 3300 (br, w, O-H), 3060 (m, C-H), 2930 (m, C-H), 1650 (vs, C=O), 1580 (s, ar), 1500 (s, ar), 1455 (vs, ar), 1250 (vs, C-O-C) cm^{-1}. δ ^1H ($CDCl_3$) 5.21 (s, 2H, -CH_2Ph), 6.88 (t, J = 7.8 Hz, 1H, H_5), 7.17 (dd, J = 1.4 and 7.8 Hz, 1H, H_4), 7.22 (dd, J = 1.4 and 7.8 Hz, 1H, H_6), 7.32 - 7.47 (m, 5H, -C_6H_5), 9.93 (s, 1H, -CHO) and 11.11 (s, 1H, -OH) ppm. δ ^{13}C ($CDCl_3$) 71.5, 119.4, 121.1, 125.3, 127.4, 128.0, 128.6, 128.6, 136.5, 147.2, 152.3 and 196.4 ppm. m/e (EI) 228 (M^+, 46), 229 (8), 227 (14) and 91 (100 %) amu. Accurate mass. Found: 228.0784; $C_{14}H_{12}O_3$ requires 228.0786 amu.

1,3-Dibenzyloxybenzene, **10**.

10 was afforded in 63 % yield by a procedure identical to the one described for **1**. Recrystallization from ethanol afforded colourless crystals, m.p. 71.0 - 72.5 °C. Elemental analysis. Found: C, 82.65; H, 6.17. $C_{20}H_{18}O_2$ requires C, 82.73; H, 6.25 %. ν_{max} ($CHCl_3$) 3060 - 3000 (m, C-H), 2920 (m, C-H), 1590 (vs, ar), 1490 (vs, ar), 1450 (s, ar) and 1260 (s, C-O-C) cm^{-1}. δ ^1H ($CDCl_3$) 5.06 (s, 4H, 2x -CH_2Ph), 6.62 (dd, J = 2.3 and 8.2 Hz, 2H, H_4 and H_6), 6.66 (t, J = 2.3 Hz, 1H, H_2), 7.21 (t, J = 8.2 Hz, 1H, H_5) and 7.34 - 7.46 (m, 10H, 2x -C_6H_5) ppm. δ ^{13}C ($CDCl_3$) 70.0, 102.3, 107.4, 127.4, 127.8, 128.5, 129.8, 136.9 and 160.0 ppm. m/e (EI) 290 (M^+, 11), 291 (2.3) and 91 (100 %) amu. Accurate mass. Found: 290.1306; $C_{20}H_{18}O_2$ requires 290.1307 amu.

2,4-Dibenzyloxybenzaldehyde, **11**.

11 was afforded in 96 % yield by a procedure identical to the one described for **2**. Recrystallization from ethanol afforded analytically pure material as white crystalline material, m.p. 83.0 - 84.0 °C. Elemental analysis. Found: C, 78.75; H, 5.55. $C_{21}H_{18}O_3$ requires C, 79.22; H, 5.70 %. ν_{max} (KBr) 3060 - 3030 (w, C-H), 2920 (w, ar), 2840 (w, CHO), 2760 (w, CHO), 1670 (s, C=O), 1610 (vs, ar), 1575 (s, ar), 1500 (m, ar), 1450 (m, ar) and 1260 (vs, C-O-C) cm^{-1}. δ ^1H ($CDCl_3$) 5.12 (s, 2H, $-CH_2Ph$), 5.15 (s, 2H, $-CH_2Ph$), 6.61 (d J = 2.2 Hz, 1H, H_3), 6.65 (dd, J = 2.2 and 8.6 Hz, 1H, H_5), 7.36 - 7.44 (m, 10H, 2x $-C_6H_5$), 7.85 (d, J = 8.6 Hz, 1H, H_6) and 10.40 (s, 1H, -CHO) ppm. δ ^{13}C ($CDCl_3$) 70.3, 70.4, 100.1, 107.0, 119.5 127.2, 127.5, 128.2, 128.3, 128.7, 128.7, 128.7, 130.4, 135.9, 162.7, 165.1 and 188.1 ppm. m/e (EI) 318 (M^+, 13), 319 (3), 289 (5) and 91 (100 %) amu. Accurate mass. Found: 318.1253; $C_{21}H_{18}O_3$ requires 318.1256 amu.

4-Benzyloxy-2-hydroxybenzaldehyde, **12**.

12 was afforded in 94 % yield by a procedure identical to the one described for **3**. Recrystallization from ethanol afforded a white crystalline material, m.p. 77.0 - 78.0 °C. Elemental analysis. Found: C, 73.85; H, 5.25. $C_{14}H_{12}O_3$ requires C, 73.67; H, 5.30 %. ν_{max} (KBr) 3600 - 3300 (m, br, O-H), 3030 (w, C-H), 2940 (w, C-H), 2840 (w, CHO), 2750 (w, CHO), 1630 (vs, C=O), 1570 (s, ar), 1500 (s, ar) and 1450 (m, ar) cm^{-1}. δ ^1H ($CDCl_3$) 5.12 (s, 2H, $-CH_2Ph$), 6.52 (d, J = 2.3 Hz, 1H, H_3), 6.63 (dd, J = 2.3 and 8.6 Hz, 1H, H_5), 7.39 - 7.43 (m, 5H, $-C_6H_5$), 7.45 (d, J = 8.6 Hz, 1H, H_6), 9.73 (s, 1H, -CHO) and 11.48 (s, 1H, -OH) ppm. δ ^{13}C ($CDCl_3$) 70.4, 101.7, 108.9, 113.6, 115.4, 127.5, 128.4, 128.7, 135.2, 135.7, 164.4 and 194.3 ppm. m/e (EI) 228 (M^+, 15), 229 (2.6) and 91 (100 %) amu. Accurate mass. Found: 228.0784; $C_{14}H_{12}O_3$ requires 228.0786 amu.

1,4-Dibenzyloxybenzene, **13**.

13 was afforded in 74 % yield by a procedure identical to the one described for **1**. Recrystallization from ethanol afforded white crystalline flakes, m.p. 125.0 - 126.0 °C. Elemental analysis. Found: C, 82.96; H, 6.29. $C_{20}H_{18}O_2$ requires C, 82.73; H, 6.25 %. ν_{max} ($CHCl_3$) 3060 (m, C-H), 2900 (s, C-H), 1610 (w, ar), 1510 (vs, ar), 1470 (s, ar), 1455 (s, ar) and 1250 (vs, C-O-C) cm^{-1}. δ ^1H ($CDCl_3$) 5.04 (s, 4H, 2x $-CH_2Ph$), 6.94 (s, 4H, H_2, H_3, H_4 and H_5), 7.34 - 7.47 (m, 10H, 2x $-C_6H_5$) ppm. δ ^{13}C ($CDCl_3$) 70.6, 115.8, 127.4, 127.8, 128.5, 137.3 and 153.2 ppm. m/e (EI) 290 (M^+, 17), 291 (4) and 91 (100 %) amu. Accurate mass. Found: 290.1306; $C_{20}H_{18}O_2$ requires 290.1307 amu.

2,5-Dibenzyloxybenzaldehyde, **14**.

14 was afforded in 89 % yield by a procedure identical to the one described for **8**, starting from 2,5-dihydroxybenzaldehyde. Recrystallization from ethanol afforded analytically pure material as yellowish needles, m.p. 90.0 - 92.0 °C. Elemental analysis. Found: C, 79.17; H, 5.70. $C_{21}H_{18}O_3$ requires C, 79.22; H, 5.70 %. ν_{max} (KBr) 3060 - 3030 (s, C-H), 2940 - 2920 (w, C-H), 2870 (m, CHO), 2770 (w, CHO), 1680 (vs, C=O), 1605 (s, ar), 1585 (m, ar), 1490 (vs, ar) and 1455 (s, ar) cm^{-1}. δ ^1H ($CDCl_3$) 5.06 (s, 2H, $-CH_2Ph$), 5.16 (s, 2H, $-CH_2Ph$), 7.02 (d, J = 9.0 Hz, 1H, H_3), 7.20 (dd, J = 3.2 and 9.0 Hz, 1H, H_4), 7.36 - 7.43 (m, 10H, 2x -C_6H_5), 7.46 (d, J = 3.2 Hz, 1H, H_6) and 10.53 (s, 1H, -CHO) ppm. δ ^{13}C ($CDCl_3$) 70.6, 71.3, 111.8, 115.1, 124.1, 125.6, 127.3, 127.5, 128.0, 128.2, 128.5, 128.6, 136.2, 136.6, 153.0, 155.9 and 189.3 ppm. m/e (EI) 318 (M^+, 7.4), 319 (1.6) and 91 (100 %) amu. Accurate mass. Found: 318.1253; $C_{21}H_{18}O_3$ requires 318.1256 amu.

5-Benzyloxy-2-hydroxybenzaldehyde, **15**.

15 was afforded in 72 % yield by a procedure identical to the one described for **3**. Recrystallization from ethanol afforded a green yellowish crystalline material, m.p. 91.0 - 92.0 °C. Elemental analysis. Found: C, 73.62; H, 5.35. $C_{14}H_{12}O_3$ requires C, 73.67; H, 5.30 %. ν_{max} (KBr) 3600 - 3350 (w, br, O-H), 3060 (w, C-H), 2940 (w, C-H), 2860 (m, CHO), 2750 (w, CHO), 1630 (vs, C=O), 1620 (s, ar), 1590 (s, ar), 1485 (vs, ar) and 1455 (s, ar) cm^{-1}. δ ^1H ($CDCl_3$) 5.07 (s, 2H, -CH_2Ph), 6.95 (d, J = 9.0 Hz, 1H, H_3), 7.09 (d, J = 3.0 Hz, 1H, H_6), 7.23 (dd, J = 3.0 and 9.0 Hz, 1H, H_4), 7.38 - 7.43 (m, 5H, -C_6H_5), 9.84 (s, 1H, -CHO) and 10.67 (s, 1H, -OH) ppm. δ ^{13}C ($CDCl_3$) 71.1, 117.0, 118.7, 120.1, 126.1, 127.4, 128.2, 128.7, 136.5, 151.8, 156.3 and 196.0 ppm. m/e (EI) 228 (M^+, 5.4), 229 (1), 137 (2) and 91 (100 %) amu. Accurate mass. Found: 228.0784; $C_{14}H_{12}O_3$ requires 228.0786 amu.

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